PATENT COOPERATION TREATY

COPY

From the:
INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	18 MAR 2005
Applicant's or agent's file reference 124199x355	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/NZ2004/000267	26 October 2004	24 October 2003

International Patent Classification (IPC) or both national classification and IPC
Int. Cl. [7] A61K 31/4184, 31/366, A61P 33/10, 33/14

Applicant
AGRESEARCH LIMITED et al

1. This opinion contains indications relating to the following items:

- [X] Box No. I Basis of the opinion
- [ ] Box No. II Priority
- [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV Lack of unity of invention
- [X] Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI Certain documents cited
- [ ] Box No. VII Certain defects in the international application
- [ ] Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing
      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format
      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in the international application as filed.
      ☐ filed together with the international application in computer readable form.
      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	YES
	Claims 1-27	NO
Inventive step (IS)	Claims	YES
	Claims 1-27	NO
Industrial applicability (IA)	Claims 1-27	YES
	Claims	NO

2. Citations and explanations:

D1. AU 52162/96 A (694016) (Virbac Australia Pty. Ltd.) 21 November 1996

D2. Hennesy, D.R. "Modifying the formulation or delivery mechanism to increase the activity of anthelmintic compounds." Veterinary Parasitology, 1997 Nov; 72(3-4): 367-82;

D3. Awadzi K, Addy ET, Opoku NO, Plenge-Bonig A, Buttner DW. "The chemotherapy of onchocerciasis XX: ivermectin in combination with albendazole." Trop Med Parasitol. 1995 Dec; 46(4): 213-20.

D4. Grimshaw WT, Hong C, Webster R, Hunt KR. "Development of immunity to lungworm in vaccinated calves treated with an ivermectin sustained release bolus or an oxfendazole pulse release bolus at turnout." Vet Parasitol. 1996 Mar; 62(1-2): 119-24.

D5. Larsen JW, Vizard AL, Anderson N. "Production losses in Merino ewes and financial penalties caused by trichostrongylid infections during winter and spring." Aust Vet J. 1995 Feb; 72(2): 58-63

D6. Anderson N and Laby RH. "Activity against Ostertagia ostertagi of low doses of oxfendazole continuously released from intraruminal capsules in cattle." Aust Vet J. 1979 May; 55(5):244-6.

Novelty (N): Claims 1-27

D1 discloses synergistic compositions of benzimidazoles and abamectin as anthelmintics including nematocidal compositions.

D2 discloses an extended release liposomal delivery system (e.g. oral tablets and intraruminal capsules) for treating sheep. At page 377, 4th paragraph, avermectin and milbemycin are given as ideal candidates.

D3 discloses a combination of the macrocyclic lactone, ivermectin, with a benzimidazole such as albendazole.

D4 discloses an ivermectin sustained release bolus as an anthelmintic, especially for the control of mites, lice and warbles. Ivermectin consists of about 80% of 22,23-dihydroavermectin B1a and 20% of 22,23-dihydroavermectin B1b, and therefore consists of 2 active agents.

D5 discloses treating sheep with a combination of ivermectin and a controlled release capsule of albendazole.

D6 discloses continuous release oxfendazole in an oral dose of 2.5mg/kg oxfendazole released at either 0.29mg/kg or 0.48mg.kg, that is, released over 5 to 8 days (see page 1, column 2, "Results"). The oxfendazole is in combination with stearic acid, polyethylene glycol and alcohol ethoxylate emulsifier.

The above citations, separately and in obvious combination, disclose mixtures of active anthelmintic agents, many being antibiotics, They include controlled release capsules and boluses of these anthelmintics. D6, in particular, specifies release over 5 to 8 days, in the range of the present application of 3 to 14 days. In D6, the other components of the oral dose, may well be considered active. A light of these citations, the alleged invention cannot be considered novel.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

Inventive Step (IS): claims 1-27

As for Novelty. In light of D1 to D6, it cannot be considered an inventive step to formulate a mixture of any 2 active ingredients, where the constituents are active for any purpose, e.g. therapeutic or nutritional, in a form that is released over 3 to 14 days. The person skilled in the art would easily formulate the composition so that it released in this time frame, as it is in D6.

Industrial Applicability (IA) Claims 1-27

Methods of treating animals and delivery devices for use in treating animals are industrially applicable.